REMARKS

Claims 1, 4-8, and 11-16 are pending in the present application.

At the outset, Applicants wish to thank Examiner Baum for the helpful and courteous discussion with their undersigned Representative on July 12, 2006. During this discussion the amendments and remarks set forth herein were discussed. Reconsideration of the remaining rejections is respectfully requested in view of the amendments and remarks set forth herein.

The rejections of Claims 1-11 under 35 U.S.C. §112, first paragraph (written description), are obviated in part by amendment and traversed in part.

Based on the outstanding Office Action and the discussion with the Examiner, the bases for this ground of rejection appear to be four-fold and are summarized by the following allegations by the Examiner:

1) the term "basic" amino acid is not defined, and
2) the absence of a recited sequence for the various members of the GRAS family,
3) the breadth of sequences having the motif defined in SEQ ID NO: 5, and
4) the lack of an apparent conserved biochemical function between the various members of the GRAS family.

With respect to criticism (1), Applicants submit that the skilled artisan would immediately appreciate the fact that the term "basic" amino acid as used in biochemistry refers to arginine, lysine, and histidine. In fact, the reference cited by the Examiner (Campbell et al) establishes this very fact. Therefore, this criticism is without merit and should be withdrawn.

In regard to criticism (2), Applicants remind the Examiner that an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." (*In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)). (MPEP § 2163.02)) Applicants further remind the Examiner that information which is well known in the art need not be described in detail in the specification. (See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). (MPEP § 2163))

To this end, Applicants again submit that the GRAS family is a well known family of proteins and that members of this family would be readily apparent to the skilled artisan. Applicants submit that the "GRAS family" (also known as the VHIID family) was already known at the time of the present invention. Further, this family is characterized by several conserved motifs. To demonstrate the state of the art that existed at the time of the present invention Applicants submitted with the response filed on December 28, 2005, two references discussed on pages 2-3 of the present application as they relate to the description of the GRAS family. These references are:

1) Pysh et al, *The Plant Journal* (1999) **18**(1), 111-119; and

2) Schumacher et al, *Proc. Natl. Adad. Sci. USA* (1999) **96**, 290-295.

Applicants further direct the Examiner's attention to *Capon v. Eshhar* (418 F.3d 1349, 76 USPQ2d 1078 (Fed. Cir. 2005) from which it is apparent that compliance with the written description requirement does not require Applicants to disclose all sequences in a genus where the members of the same would be readily apparent to the skilled artisan (i.e., the members are within the state of the knowledge in the art). Therefore, criticism (2) by the Examiner is also without merit.

Moreover, referring to criticism (3), Applicants note that the claims actually are directed to a particular sub-set of members of GRAS proteins, i.e., a GRAS protein having a motif defined by SEQ ID NO: 5. Therefore, the claims do not read on any polynucleotide that encodes any protein that contains SEQ ID NO: 5 as the Examiner seems to imply, but rather the protein must also be a member of the GRAS family. Therefore, the analysis should be a two-step analysis. First, the protein sequence is evaluated to determine whether it is a GRAS family protein based on the well delineated sequence-based family characteristics. Second, if the protein sequence is a GRAS family protein, then the proteins will be evaluated to determine whether SEQ ID NO: 5 is present therein. Only where both of these steps are affirmatively answered would the sequence be within the scope of the claimed invention. As such, the description in the specification and the skill level in the relevant art is sufficient to clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.

In this light, the Examiner is reminded that the presence of the peptide motif of sequence (I) further defines the members of the GRAS family from which the mutants of the present invention can be obtained. This motif (GYRVEEE or GYNVEE) is present only in a sub-group of GRAS proteins that are involved in regulation of plant size. The sequence alignment shown in Figure 1 of the present application shows that this motif is present in BZH, GAI, RGA, and RGAL proteins, each of which are involved in the regulation of plant height. In contrast, this motif is not found in SCR, which is involved in radial patterning of the roots, or LS which is involved in shoot branching. Peng et al, *Nature* (1999) **400**, 256-261, which discloses GRAS proteins involved in regulation of plant size in wheat and maize and which containing the GYRVEE sequence (maize d8) or a closely related sequence (GYKVEE in the case of wheat Rht-1).

The mutants of the present invention are defined by a mutation in the aforementioned conserved sequence, namely, by a substitution of the C-terminal glutamic acid by a basic amino acid. Due to the high degree of conservation of this glutamic acid residue in GRAS proteins involved in the regulation of plant size, it is highly probably that the same mutation in any of these proteins will result in a reduction of the plant size.

In discussing the foregoing on page 4 of the Office Action, the Examiner asserts that GAI and RGA are "not homologous genes, as evidenced by their names", and that the corresponding proteins have different biochemical activities. This assertion appears to be based only on the names of these proteins, but this allegation by the Examiner is incorrect.

First, Applicants wish to point out that it is not reported in the publication of SHUMACHER *et al.* that "RGA" means: "Repressor of GAI", but that "RGA" means: "Repressor of GAl-3". Further, the name of these genes is not a description of the biochemical function of the wild-type proteins that they encode. Actually, they were named from phenotypic characteristics of mutant alleles.

"Gibberellin insensitive" refers to a gain-of-function mutation which was found to confer a dwarf phenotype, not reversed by GA (see publication of Peng *et al.*, 1997 cited in the previous Office Action). "Repressor of GA1-3" refers to a loss-of-function mutant, which was found to be a recessive suppressor of the dwarfism of the GA-deficient *gal-3* mutant (see the publication of Silverstone *et al.*, 1998; **submitted herewith** as Annex 1). Peng *et al.* and Silverstone *et al.* describe GAI and RGA as "negative regulators of gibberellin response", and Silverstone *et al.* clearly state (see Discussion) that they are homologous.

Further, it has been confirmed that gain-of-function mutations of RGA and RGAL confer a GA insensitive dwarf phenotype similar to the phenotype conferred by gain-of-

function mutations of GAI (see abstracts of Wen & Chang 2002, and Dill *et al.*, 2001, in the list of abstracts **submitted herewith** as Annex 2).

Applicants also **submit herewith** (Annex 3) a copy of a publication of Olszewski *et al.*, which reports that GAI and RGA belong to a same family, and that all the members of the GAI/RGA family are negative regulators of GA perception and response (pages S68 to S70). The GAI/RGA family is also known as "DELLA family", by reference to a conserved amino-acid motif which is found in these proteins and not in the other members of the GRAS family.

Applicants also **submit herewith** (Annex 4) a copy of a page from the Expasy website (www.expasy.org), which provides a list of representative members of the DELLA family. Annex 5 **submitted herewith** provides the sequences of the listed proteins, wherein the positions of the DELLA motif and of the GYRVEE, GYRVEE or GYKVEE sequences have been highlighted. Semi-dominant mutants with dwarf phenotypes have been described for many of these proteins (cf. the publications of Peng *et al.* previously cited, and the abstracts listed in Annex 2) i.e Q9LQT8 (Arabidopsis thaliana GAI), Q9SLH3 (Arabidopsis thaliana RGA), Q9C8Y3 (Arabidopsis thaliana RGL1), Q9ST59 (Wheat RHT-1), Q9ST48 (maize dwarf 8), Q8S4W7 (Grape VvGAI1), Q5BN23 (Brassica campestris BrRGA1), Q8W127 (Barley SLN1), Q7G7J6, (Rice SLR1).

Annex 6, **submitted herewith**, is a copy of the publication of Muangprom *et al.* The Brrga1-d mutant disclosed in this publication is not the same as the mutants of the invention. However, it is somewhat similar in that it induces a similar phenotype, and that it also results from a single amino-acid substitution in a sequence which is highly conserved between proteins of the GAI/RGA family, and which is located in the C-terminal region.

In view of the foregoing, Applicants submit that criticism (3) by the Examiner is also without merit.

Finally, in regard to criticism (4) and to further reinforce the foregoing, Claim 1 has been amended to specify that the activity of the members of the GRAS family within the scope of the claimed invention is to impart upon a plant transformed with and expressing the same a phenotype of reduced plant height compared to the wild-type plant. As such, Applicants submit that criticism (3) by the Examiner is now without merit.

In view of the foregoing, Applicants submit that the specification provides an adequate description, when coupled with the state of the art at the time of the present invention, to allow the skilled artisan to recognize what has been invented. As such, what is claimed is adequately described in the specification within the meaning of 35 U.S.C. § 112, first paragraph.

Withdrawal of this ground of rejection is requested.

The rejections of Claims 1, 4-8, and 11 under 35 U.S.C. §112, first paragraph (enablement), is respectfully traversed.

The Examiner's criticism in this regard focused largely on the lack of an apparent conserved biochemical function between the various members of the GRAS family. Based on these apparent differences, the Examiner alleges that the skilled artisan would have no expectation that sequentially and functional discordant proteins would provide the same phenotype (e.g., reduced plant height). In making this rejection, it appears that the Examiner confused the gain-of-function and loss-of-function mutations.

Since GAI/RGA proteins are negative regulators of GA response, a loss-of-function mutation results in the production of an inactive regulator and in an increase of the GA

response, giving a "slender" mutant, with tall phenotypes. On the other hand, a gain-of-function mutation results in a protein which is more active than the wild protein (or which is always active, while the wild-type protein is degraded) and in a down-regulation of the GA response, inducing a dwarf phenotype. A more detailed explanation of the effects of gain-of-function and loss-of-function mutations in the GAI/RGA proteins can be found in the publication of Olszewski *et al.* (Annex 3).

The *bzh* mutation of the present invention is a gain-of-function mutation. The presence of a single copy of the mutated gene within a plant is sufficient to provide an increased down-regulation of the GA response, and induce dwarfism. If two copies of the mutated gene are present the dwarfism will be more marked (cf. page 6, lines 31-38 of the instant application).

Further to the foregoing, the Examiner is again reminded that MPEP §2164.04 states:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Throughout the specification, Applicants provide a detailed explanation of how the skilled artisan may clone, express, and characterize the polynucleotides that fall within the scope of the present invention. For the reasons stated above, the identification of the full scope of parent sequences containing the motif of sequence (I) would be readily apparent to the skilled artisan. Further, the information provided in the present specification with respect to the nature of the gene, the nature and position of the mutations, and the effect of this mutation (reduction in size depending on the level of expression in the plant of the mutant sequence), is sufficient to place the skilled artisan in possession of the full scope of the

present invention to reliably reproduce the same. Moreover, Applicants submit that procedures for expressing a gene in a plant were well known to the skilled artisan as of the date of the present invention. As such, the skilled artisan could reliably use the procedures available in the art for expressing the mutant gent of the present invention without undue experimentation.

MPEP § 2164.01 states:

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Applicants submit that determining what sequences fall within or without the scope of the present claims, as well as producing plants expressing the same, would be readily apparent to the skilled artisan with the present application in hand. This is especially true when the state of the art as represented by Pysh et al, Schumacher et al, and Peng et al is considered.

Based on the foregoing, Applicants submit that the present claims are fully enabled by the specification and the common knowledge available in the art and as such withdrawal of this ground of rejection is requested.

In view of the foregoing, Applicants request withdrawal of these grounds of rejection.

The rejection of Claims 14-16 under 35 U.S.C. §102(b) over Foisset et al is respectfully traversed.

The Examiner alleges that Foisset et al disclose a dwarf *Brassica napus* plant comprising a mutant *breizh* (*bzh*) gene. The Examiner's bases this allegation on the statement on page 3, lines 30-33 in the present specification. The Examiner further alleges that Applicants' claims read on an endogenous gene and not to a gene that that has been

isolated. In so doing, it appears that the Examiner considers that the citation of the publication of Foisset et al in the application amounts to an admission of this publication as anticipating prior art. Applicants disagree with this assertion and conclusion. Foisset et al is cited for what it teaches, i.e. that a dwarf rapeseed mutant obtained from chemical mutagenesis of seeds has been identified and that the underlying gene is denominated *Bzh*, and nothing more. To read further into this statement is an inaccurate assertion and lacks merit in the specification as filed.

For the reasons set forth in the response filed December 28, 2005, Foisset et al is clearly insufficient to enable one of ordinary skill in the art to reproduce the dwarf rapeseed plants. Thus the disclosure of Foisset et al does not put the public in possession of the subject matter of claims 14-16 for the reasons restated below:

The allegation that Applicants' claims read on an endogenous gene is obviated by the previous amendment to the claims to add the term "isolated." Foisset et al fail to disclose or suggest a mutant plant with reduced development set forth in Claims 14-16.

The Examiner is reminded:

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... ." *In re Hoeksema,* 399 F.2d 269, 158 USPQ 596 (CCPA 1968). The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*<, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003) (MPEP §2121.01)

The Examiner alleges that Applicants admit that the phenotype observed in Foisset et al is the result of a mutant *bzh* gene. However, Applicants submit that the Foisset et al fails to provide any evidence to suggest that the resultant dwarf phenotype is the result of a mutant

bzh gene, it is only the present invention that has isolated, characterized, and determined the link between dwarfism and the specifically claimed mutant *bzh* gene.

Foisset et al disclose that they produced a rapeseed dwarf mutant from chemical (EMS) mutagenesis. However, Applicants submit that such a disclosure is not sufficient to reproduce the claimed invention. If the skilled artisan were to follow the disclosure of Foisset et al and perform chemical mutagenesis in accordance therewith, a number of dwarf mutants would likely result. There are several genes that can be involved in dwarfism. For example, Applicants submitted Annex I attached to the response filed on December 28, 2005, which provides abstract of some publications showing that a large variety of genes belonging to the gibberellin pathway or the brassinosteroids pathway may be involved in dwarfism.

Even with the *bzh* gene there are several mutations in this gene that may induce dwarfism (e.g., mutations in the N-terminal portion of the protein as disclosed in Peng et al for *Arabidopsis gai* gene). Foisset et al disclose that the *bzh* mutation has been obtained by EMS mutagenesis of seeds. EMS mutagenesis primarily induces G→A substitutions. Therefore, the only suggestion that the skilled artisan would take from Foisset et al is that the *bzh* mutation is likely a G→A substitution. However, the size of the rapeseed genome is about 1200 x 10^6 bp. If one considers a G/C content of approximately 50%, there would be about 600 x 10^6 possible G→A substitutions genome-wide.

The only "guide" that Foisset et al provide to determine which of the 600 x 10^6 possible G→A substitutions is responsible for the *bzh* mutation is that the *bzh* mutation results in dwarfism. Foisset et al fail to provide any guidance to the skilled artisan to a homolog of the *gai* gene of *Arabidopsis*. Further, Foisset et al do not disclose or suggest that the *bzh* mutation has a characteristic of "semi-dominance" and insensitivity to gibberellins,

which are similar to those of the *gai* mutations. Only the present inventors have discovered these characteristics.

As stated above and shown in Annex I attached to the response filed on December 28, 2005, a large variety of genes, belonging to (for example) the gibberellin pathway or the brassinosteroids pathway, may be involved in dwarfism. In view of the disclosure of Foisset et al, the skilled artisan would conclude the G→A substitute responsible for the *bzh* mutation is found somewhere in one of the known or unknown genes possibly involved in dwarfism. However, there is no disclosure or suggestion in Foisset et al to direct the skilled artisan to the specific gene or the specifically claimed polynucleotide.

Accordingly, Applicants submit that in view of the disclosure of Foisset et al, the skilled artisan would not have been able to differentiate the dwarf mutant of the present invention from other dwarf mutants obtained via chemical mutagenesis, much less identify the specifically claimed gene of Claim 1 giving rise to the mutant plant of Claims 14-16.

As such, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 1, 4-8, 11, and 14-16 under 35 U.S.C. §112, second paragraph, is obviated by amendment and submission of a substitute Sequence Listing.

With respect to the Examiner's rejection of claims as being indefinite, Applicants submit that the sequence defined in Claim 1 is not incongruous with SEQ ID NO: 6 as this sequence is merely a sub-genus of SEQ ID NO: 6. However, to avoid unnecessary delays, Applicants **submit herewith** a substitute Sequence Listing adding SEQ ID NO: 7, which would correspond to SEQ ID NO: 6 having X2 as a basic amino acid.

Applicants have now submitted a substitute Sequence Listing and a corresponding computer-readable Sequence Listing. The sequence information recorded in the

corresponding computer-readable Sequence Listing is identical to the paper copy of the substitute Sequence Listing. Support for all of the sequences listed in the substitute Sequence Listing is found in the present application as originally filed. No new matter is believed to have been introduced by the submission of the substitute Sequence Listing and the corresponding computer-readable Sequence Listing.

Withdrawal of this ground of rejection is requested.

Finally, the Examiner's objection to the Declaration is obviated by the submission of the substitute Declaration **submitted herewith**. Acknowledgement that this ground of objection has been withdrawn is requested.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

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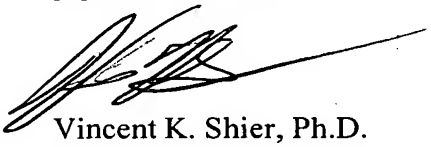

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